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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/700,816	11/04/2003	Zuoshang Xu	UMY-038	9864
959 7590 12/01/2009 LAHIVE & COCKFIELD, LLP FLOOR 30, SUITE 3000 ONE POST OFFICE SQUARE BOSTON, MA 02109			EXAMINER MCGARRY, SEAN	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 12/01/2009	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

***Advisory Action  
Before the Filing of an Appeal Brief***

**Application No.**

10/700,816

**Applicant(s)**

XU ET AL.

**Examiner**

Sean R. McGarry

**Art Unit**

1635

– ***The MAILING DATE of this communication appears on the cover sheet with the correspondence address –***

THE REPLY FILED 12 November 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.  
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
 Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 12 November 2009. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: \_\_\_\_\_.  
 Claim(s) objected to: \_\_\_\_\_.  
 Claim(s) rejected: 1,5-9,11,12,28-33,37-43 and 45-48.  
 Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: Applicant argues that the art was so unpredictable at the time of invention that one in the art would have had no expectation that following the prior art teachings would lead to allele specific inhibition via siRNA compounds. Applicant has cited several references as evidence of the unpredictability of the art at the time of invention. Applicant has not previously relied upon these references, either at all, or in the context now used. The examiner is not apt to consider these references at this point in prosecution since applicant has provided no reason why they were not provided earlier any why they are now needed. The examiner would indeed be precluded from providing rebutting evidence upon consideration of what applicant now wishes to rely upon. The Holen, Jacque et al., Yu et al., and Hamada references have not been considered in the context of applicant's assertion of unpredictability of the art. The prior art relied upon by the examiner has provided a means and motivation to provide for siRNA compounds that would provide allele specific inhibition. The prior art has shown allele specific inhibition of the very target applicant recites via antisense compounds. The prior art has shown how to make siRNA with the same activity as the prior art allele specific antisense compounds. Applicants compounds utilized in their methods are modified at the positions taught by the prior art. The prior art has provided the same motivation of treating disease caused by gain of function SOD-1 alleles. It is noted that a reasonable expectation of success is not an absolute expectation, but a reasonable one. With the prior art cited, the examiner believes that this level of expectation has been established. It is noted that applicant claims do not provide that there is no inhibition of the wt gene (the specification teaches that the wt gene is not "significantly inhibited," see page 10, for example). The claimed invention is not even limited to there only being one nucleotide difference in the compounds used in their invention. It is noted that applicant claims were previously broad enough to include the inhibition of any differing allele in a cell and the examiner made no enablement rejection at that time. The rejections of record over the instant claims is maintained for the same reasons of record.

12. ☐ Note the attached Information Disclosure Statement(s) (PTO/SR/08) Paper No(s)

/Sean R McGarry/  
Primary Examiner, Art Unit 1635